Review Article

Triterpenoids from the spores of Ganoderma lucidum

Bingji Ma, Wei Ren, Yan Zhou, Jinchuan Ma, Yuan Ruan, Chun-Nan Wen

Department of Traditional Chinese Medicine
Agronomy College of Henan Agricultural University, Zhengzhou 450002, China.

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Abstract

Recently a series of triterpenoids were isolated from ganoderma spores and have drawn the attention of chemists and pharmacists. The aim of this review is to summarize the triterpenoids and their bioactivities of ganoderma spores. The chemical and biological literatures of ganoderma spores dealing with the structural analysis and bioactivity assay were selected. Triterpenoids isolated from ganoderma spores showed significantly anti-HIV-1 protease, anti-tumor, and anti-complement activities. Triterpenoids are the main active constituents of ganoderma spores and show various bioactivities for its medicinal use. In addition, biological activities of ganoderma spores still need further assessment before they can be accepted not only by the traditional Asian medicine community, but also by western science and medicine.

Keywords: Ganoderma lucidum spores, triterpenoids, structures, bioactivities, mushroom.

Correspondence to: Professor Bingji Ma, Department of Traditional Chinese Medicine, Agronomy College of Henan Agricultural University, Zhengzhou 450002, China. Tel.: +86 37163504463, Fax: +86 37163558126, E-mail: mbj123@sina.com

Introduction

Ganoderma is a white rot wood-degrading basidiomycete with hard fruiting bodies. In traditional Chinese medicine, Ganoderma lucidum and Ganoderma japonicum are two species widely used as medicine for a variety of diseases, such as chronic bronchitis inflammation, hyperlipidemia, hypertension, neurasthenia, hepatitis, leukopenia, and adjuvant treatment of cancer [1, 2]. Ganoderma spores are the fungus's reproductive cells ejected from the cap of G. lucidum after the fruiting bodies become mature. In recent years, with the development of spores collection, sporoderm-broken technology and application of modern analysis instruments, it has made great progress on chemical constituents, pharmacological effects and mechanisms of action of Ganoderma spores. Moreover, an increasing number of publications in domestic and international journals suggest the important bioactivities of the spores of G. lucidum [3, 4].

At present, the chemical constituents and bioactivities of the fruiting bodies of G. lucidum have been fully investigated, and the triterpenoids were found to be the most important active substances for its numerous pharmacological uses. Up to now, more than 150 triterpenoids have been reported from the fruiting bodies of G. lucidum representing five major structural classes [5-8]. Compared with the fruiting bodied of G. lucidum, the deep chemically investigation of the spores of G. lucidum can only be traced to 1988 [9]. Due to recent advances in modern spectroscopic and spectrometric techniques, a series of triterpenoids were isolated from the spores of G. lucidum and have drawn the attention of chemists and pharmacists. However, to the best of our knowledge, a review on the chemistry of the compounds isolated from the spores of G. lucidum has not been prepared. As we know, all the triterpenoids in the spores of G. lucidum have the same biosynthetic pathway, namely movalonic acid pathway (MVA). They start from the trans-squalene and then were transformed by oxidation, reduction, deacidification, cyclization or rearrangement, which generates various types of triterpenoids within the spores. This paper covers the structures and biological activities of 29 triterpenoids isolated from the spores of G. lucidum since 1988 (Figure 1, Table 1).

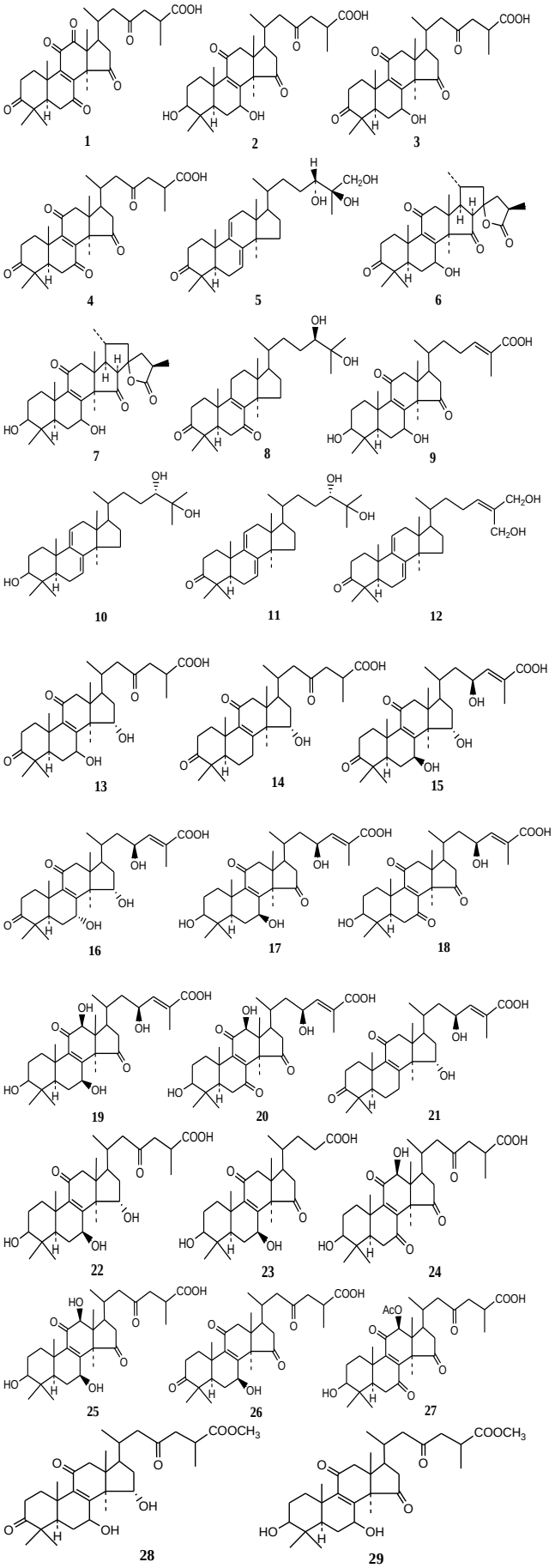

Fig. 1 Structures of triterpenoids of Ganoderma spores 1-29

Table 1 List of the triterpenoids from the spores of G. lucidum

No.	Name	Molecular formula	Molecular w.	Refs.
1	ganopsoreric acid A	$C_{30}H_{38}O_8$	526	10
2	ganoderic acid B	$C_{30}H_{44}O_7$	516	10
3	ganoderic acid C_1	$C_{30}H_{42}O_7$	514	10
4	ganoderic acid E	$C_{30}H_{40}O_7$	512	10
5	ganodermanontriol	$C_{30}H_{48}O_4$	472	10
6	ganosporelactone A	$C_{30}H_{40}O_7$	512	11
7	ganosporelactone B	$C_{30}H_{42}O_7$	514	11
8	lucidumol A	$C_{30}H_{48}O_4$	472	12
9	ganoderic acid β	$C_{30}H_{44}O_6$	500	12
10	lucidumol B	$C_{30}H_{50}O_3$	458	12
11	ganodermanondiol	$C_{30}H_{48}O_3$	456	12
12	ganoderiol F	$C_{30}H_{46}O_3$	454	12
13	ganoderic acid A	$C_{30}H_{44}O_7$	516	12
14	ganolucidic acid A	$C_{30}H_{44}O_6$	500	12
15	ganoderic acid γ	$C_{30}H_{44}O_7$	516	13
16	ganoderic acid δ	$C_{30}H_{44}O_7$	516	13
17	ganoderic acid ε	$C_{30}H_{44}O_7$	516	13
18	ganoderic acid ξ	$C_{30}H_{42}O_7$	514	13
19	ganoderic acid η	$C_{30}H_{44}O_8$	532	13
20	ganoderic acid θ	$C_{30}H_{42}O_8$	530	13
21	ganolucidic acid D	$C_{30}H_{44}O_6$	500	13
22	ganoderic acid C_2	$C_{30}H_{46}O_7$	518	13
23	lucidenic acid SP1	$C_{27}H_{40}O_6$	460	14
24	ganoderic acid C_6	$C_{30}H_{42}O_8$	530	14
25	ganoderic acid G	$C_{30}H_{44}O_8$	532	14
26	ganoderic acid D	$C_{30}H_{42}O_7$	514	15
27	ganoderic acid H	$C_{32}H_{44}O_9$	572	15
28	methyl ganoderate A	$C_{31}H_{48}O_7$	530	16
29	methyl ganoderate B	$C_{31}H_{48}O_7$	530	16

Triterpenoids Isolated From The Spores Of G. Lucidum

Five triterpenoids were islolated from the ether-soluble fraction of spores of G. lucidum and on the basis of chemical properties and spectral data, they were identified as ganopsoreric acid A (1), ganoderic acid B (2), ganoderic acid C_1 (3), ganoderic acid E (4) and ganodermanontriol (5), respectively. Pharmacological experiments showed that ganopsoreric acid A had an activity for lowing the levels of GTP in mice with the liver injured by CCl_4 and GaNI [10]. Two new pentacyclic triterpenoids, named ganosporelactone A (6) and B (7) were isolated from the spores of G. lucidum, which may be biogenetically derived from the lanostane skeleton through the construction of C_{18} and C_{23} bond [11]. Two new lanostane-type triterpenes, lucidumol A (8) and ganoderic acid β (9), togather with a new natural one lucidumol B (10) and seven known triterpenoids, ganodermanondiol (11), ganoderiol F (12), ganoderic acid A (13), ganolucidic acid A (14), and 2, 3, 5. Of the compounds isolated, compounds 5, 10, 11 and 14 showed significant anti-human immunodeficiency virus (anti-HIV)-1 protease activity with IC_{50} values of 20-90 μM [12].

Six new highly oxygenated lanostane-type triterpenes, called ganoderic acid γ (15), ganoderic acid δ (16), ganoderic acid ε (17), ganoderic acid ξ (18), ganoderic acid η (19), ganoderic acid θ (20), together with

ganolucidic acid D (21) and ganoderic acid C_2 (22) were isolated from the Ganoderma spores. The cytotoxicity of the compounds 15-21 was carried out in vitro against Meth-A and LLC tumor cell lines [13]. A new highly oxygenated C_{27} terpenoid, lucidenic acid SP1 (23), was isolated from a $CHCl_3$-soluble fraction of G. lucidum spores together with eleven triterpenoids, namly, ganoderic acid C_6 (24), ganoderic acid G (25), and 2, 3, 5, 8, 9, 11, 12, 13, 14. These twelve compounds were investigated in vitro for their anticomplementary activity. Compounds 5, 11 and 12 showed a strong anticomplement activity against the classic pathway (CP) of the complement system with IC_{50} values of 4.8, 17.2 and 41.7μM, respectively [14]. In addition, Zhang first reported two known triterpenoids, ganoderic acid D (26) and ganoderic acid H (27) from the spores of G. lucidum [15]. Zhang first isolated another two triterpenoids, methyl ganoderate A (28) and methyl ganoderate B (29) from the same fungus' spores [16].

Conclusions

Some progress of chemical and pharmacological research has been made on the spores of G. lucidum. In some cases, extracts of partly-purified preparations and pure compounds from Ganoderma spores have been used for in vitro or in vivo testing [17, 18], however, there are still some difficulties to be overcome before Ganoderma spores become a modern drug, these being:

i) Ganoderma spores are expensive, and the extraction rate is too low, and usually not more than 5%. In addition, there is a dispute whether the sporoderm-broken spores of G. lucidum can improve the effect used in the clinical trials [19]; ii) Triterpenoids are often mixed with fatty acids in the bodies of Ganoderma spores, both of them are low polar components, so the isolation of triterpenoids presents more difficulties than the other chemical constituents; iii) The pharmacological studies on triterpenoids of Ganoderma spores are still not enough, and the interrelation of Ganoderma spores' various pharmacological activities need to be elucidated; and iv) As the biological activities of Ganderma spores are determined by the active ingredients contained, the levels of active ingredients vary from the origin, cultivation, acquisition time and extraction methods. For example, four triterpenoids of Ganoderma spores from different areas showed obviously different results in the content reported by Ma [20]. Furthermore, the inhibition of NF-Kb, and the inhibition of cell migration of MDA-MB-231 and PC-3 are not of the same intensity among different sources of Ganoderma spores [21].

At present, the spores of G. lucidum have been widely used in China, and its medical value has been widely recognized, however, its biological activities need further assessment before they can be accepted not only by the traditional Asian medicine community, but also by western science and medicine. Modern biotechnological cultivation method in bioreactors enable fast, efficient and economical production of Ganoderma spore biomass in sufficient quantities for potential further pharmaceutical industrial production.

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